

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 20-870

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-870

Rhone Poulenc Rorer
Attention: John J. Savarese, M.D., Ph.D.
Director, Regulatory Affairs
500 Arcola Road
P.O. Box 1200
Collegeville, PA 19427-0107

Dear Dr. Savarese:

Please refer to your new drug application (NDA) dated August 7, 1997, received August 7, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for CombiPatch™ (estradiol/norethindrone acetate) transdermal system 0.05/0.14 mg per day and 0.05/0.25 mg per day.

We acknowledge receipt of your submissions dated August 7, September 23, October 8, 17 and 28, November 6, December 4 (2), 1997; February 6, 11 and 27, June 12 (2), 13, 16, 17, 22, 23 and 24, July 6, 15 (2), 16, 23, and 29, and August 3, 4, 5, and 6, 1998. The user fee goal date for this application is August 7, 1998.

This new drug application provides for the use of CombiPatch (estradiol/norethindrone acetate) transdermal system for the treatment, in women with a uterus, of:

1. moderate-to-severe vasomotor symptoms associated with menopause;
2. vulvar and vaginal atrophy; and
3. hypoestrogenism due to hypogonadism, castration or primary ovarian failure.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (package insert, patient package insert, immediate container and carton labels dated August 6, 1998). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 20-870." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitments specified in your submission dated August 5, 1998. These commitments, along with any completion dates agreed upon, are listed below:

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.82(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

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Please submit one market package of the drug product when it is available.
We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact John C. Markow, Project Manager, at (301) 827-4260.

Sincerely,

/S/

Lisa D. Rarick, M.D.

Director

Division of Reproductive and Urologic Drug Products

Office of Drug Evaluation II

Center for Drug Evaluation and Research

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cc:

Archival NDA 20-870

HFD-580/Div. Files

HFD-580/JCM

HF-2/MedWatch (with labeling)

HFD-002/ORM (with labeling)

HFD-102/ADRA (with labeling)

HFD-40/DDMAC (with labeling)

HFD-613/OGD (with labeling)

HFD-21/ACS (with labeling) - for drug discussed at advisory committee meeting.

HFD-95/DDMS (with labeling)

HFD-820/DNDC Division Director

DISTRICT OFFICE

Drafted by: JCM/August 5, 1998

filename: 20870AP.LET

(APPROVAL (AP) (with Phase 4 Commitments)